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Decreased Expression of *IFNG-AS1*, *IFNG* and *IL-1B* Inflammatory Genes in Medicated Schizophrenia and Bipolar Patients

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Abstract

Although aberrant expression of cytokines such as IL-1B and IFNG in blood from psychiatric patients supports a role of inflammation in the pathogenesis of the disease, little is known about mechanisms underlying their regulation. We aimed to evaluate the putative role of *IFNG-AS1* long non-coding RNA (lncRNA) in controlling of *IFNG* locus in patients with schizophrenia (SZ) and bipolar (BP). We analysed the expression levels of *IFNG-AS1* long non-coding RNA, and *IFNG* and *IL-1B* mRNAs in blood cells from 27 SZ- and 30 BP-medicated patients and in 32 healthy controls. Our data showed that *IFNG-AS1* expression dramatically decreased in BP and SZ patients compared with controls and was significantly correlated with *IFNG* expression in patients specifically. Transcript levels of *IL-1B* were also significantly reduced in BP and SZ patients compared with controls. No significant differences in the expression of *IFNG-AS1, IFNG* and *IL-1B* genes were found between patients with BP and SZ. Our data shed further light on the potential role of inflammation, and more particularly inflammatory lncRNAs, in SZ and BP diseases and their pharmacological treatment.

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Introduction

Schizophrenia (SZ) and bipolar (BP) disorders are clinically and aetiologically heterogeneous debilitating chronic psychiatric diseases. Several studies have revealed that both genetics and environmental factors are involved in the pathogenesis of SZ and BP [1]. Despite marked differences in the aetiology and clinical course between BP and SZ diseases, they share common features regarding underlying genetic loci and gene expression changes [2, 3]. Inflammation and infections have been implicated in the pathogenesis of SZ [4] and BP [5], and dysregulated levels of inflammatory molecules and cytokines were found in peripheral blood from patients with SZ and BP [6]. IL-1β is a pro-inflammatory cytokine secreted by a variety of cells such as peripheral and brain macrophages (monocytes, microglial cells), astrocytes and brain endothelial cells and is a known pro-inflammatory mediator of inflammatory reactions of the central nervous system (CNS) [7]. IL-1β involvement in the pathogenesis of psychiatric disease such as SZ and BP likely arises from its effect on the development of the neurotransmitter systems [8, 9] and its contribution to neuroimmune and neuroinflammatory processes, the latter *via* activation of other immune cells such as peripheral and CNS-resident macrophages and T cells, disruption of the blood–brain barrier (BBB) and subsequent alteration of the brain functions [10, 11]. Another important inflammatory mediator, which was found dysregulated in SZ and BP [12, 13] and may affect the immune-related pathogenesis of SZ and BP, is interferon-gamma (IFN-γ). IFN-γ is a pro-inflammatory cytokine mostly produced peripherally by pro-inflammatory Th1 T lymphocytes and NK cells but also centrally within the CNS by neurons and glial cells [14]. In addition to its role in microglia-mediated neuronal dysfunction [15], IFN-γ may affect the brain function by directly altering neuronal circuits [16], synaptic plasticity [17, 18] or the kynurenine pathway [19]. Importantly, genetic variation of the *IFNG* gene has been associated with risk to develop SZ and BP [20–22]. However, the molecular mechanisms underlying cytokine expression involved in

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